AMENDMENTS TO THE CLAIMS

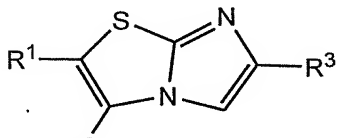
This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method of ~~inhibiting~~ reducing cell death in a mammal, wherein the method comprises administering to a mammal an effective amount of a composition comprising a cell protection factor covalently linked to a bone targeting agent via a linkage that is cleaved under physiological conditions, whereby the cell protection factor is released from the bone targeting agent *in vivo* to ~~inhibit~~ reduce cell death in bone marrow cells.

2. (Original) The method of claim 1, wherein the cell protection factor is a temporary p53 inhibitor.

3-5. (Canceled)

6. (Original) The method of claim 2, wherein the cell protection factor is a compound of Formula IV:



(IV)

wherein R^1 and R^2 are taken together to form an aliphatic or aromatic carbocyclic 5- to 8-membered ring, optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties, and

R^3 is selected from the group consisting of a C_1-C_6 alkyl group, a C_1-C_6 alkoxy group, and a phenyl group, wherein the alkyl group, the alkoxy group, or the phenyl group is optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties.

7. (Original) The method of claim 6, wherein R^1 and R^2 are taken together to form a 5- or 6-membered aliphatic carbocyclic ring optionally substituted with one or more C_1-C_6 alkyl groups.

8 -11. (Canceled).

12. (Currently Amended) The method of claim1, wherein the cell death ~~to be inhibited~~ is caused by exposure to at least one chemical or radiation.

13 -16. (Canceled).

17. (Original) The method of claim 1, wherein the mammal comprises at least one tumor.

18. (Original) The method of claim 17, wherein the mammal comprises at least one $p53^+$ tumor.

19. (Original) The method of claim 6, wherein the mammal comprises at least one tumor.

20. (Original) The method of claim 19, wherein the mammal comprises at least one $p53^+$ tumor.

21 - 22. (Canceled).

23. (Original) The method of claim 1, wherein the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide.

24. (Canceled).

25. (Original) The method of claim 6, wherein the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide.

26. (Canceled).

27. (Previously Presented) The method of claim 1, wherein the linkage is an acid-cleavable linkage.

28. (Canceled).

29. (Previously Presented) The method of claim 6, wherein the linkage is an acid-cleavable linkage.

30. (Canceled).

31. (Previously Presented) The method of claim 27, wherein the linkage is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

32. (Canceled).

33. (Previously Presented) The method of claim 29, wherein the linkage is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

34. (Canceled).

35. (Previously Presented) The method of claim 1, wherein the linkage is a hydrolytically cleavable linkage.

36. (Previously Presented) The method of claim 1, wherein the linkage is cleaved enzymatically cleavable.

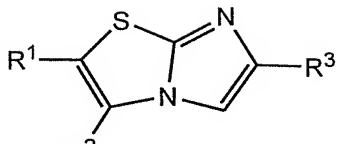
37. (Original) The method of claim 1, wherein the mammal is a human.

38-74. (Canceled).

75. (Previously Presented) The method of claim 7, wherein the cell protection factor is pifithrin-β.

76. (Currently Amended) A method of ~~inhibiting~~ reducing cell death in a mammal, wherein the method comprises administering to a mammal an effective amount of a composition comprising a cell protection factor covalently linked to a bone targeting agent via a linkage that is cleavable under physiological conditions,

wherein the cell protection factor is a compound of Formula IV:



(IV)

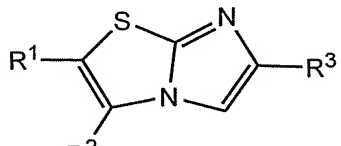
wherein R^1 and R^2 are taken together to form an aliphatic or aromatic carbocyclic 5- to 8-membered ring, optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties, and

R^3 is selected from the group consisting of a C_1-C_6 alkyl group, a C_1-C_6 alkoxy group, and a phenyl group, wherein the alkyl group, the alkoxy group, or the phenyl group is optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties;

whereby the cell protection factor is released from the bone targeting agent *in vivo* to ~~inhibit~~ reduce cell death, wherein the cell protection factor is a temporary inhibitor of a tumor suppressor gene, the bone targeting agent is a ligand that binds hydroxyapatite, and the linkage is an organic moiety comprising a nucleophilic or electrophilic reacting group which allows covalent linking to the bone targeting agent.

77. (Currently Amended) A method of ~~inhibiting~~ reducing cell death in a mammal, wherein the method comprises administering to a mammal an effective amount of a composition comprising a cell protection factor covalently linked to a bone targeting agent via a linkage that is cleavable under physiological conditions, whereby the cell protection factor is released from the bone targeting agent *in vivo* to ~~inhibit~~ reduce cell death, wherein:

wherein the cell protection factor is a compound of Formula IV:



(IV)

wherein R^1 and R^2 are taken together to form an aliphatic or aromatic carbocyclic 5- to 8-membered ring, optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties, and

R^3 is selected from the group consisting of a C_1-C_6 alkyl group, a C_1-C_6 alkoxy group, and a phenyl group, wherein the alkyl group, the alkoxy group, or the phenyl group is optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties;

the cell protection factor is a temporary p53 inhibitor;

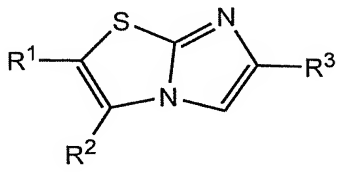
the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide; and

the linkage is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

78. (Canceled)

79. (New) A method of reducing cell death in a mammal, wherein the method comprises administering to a mammal an effective amount of a composition comprising a temporary p53 inhibitor cell protection factor covalently linked to a bone targeting agent via a linkage that is cleavable under physiological conditions, whereby the cell protection factor is released from the bone targeting agent *in vivo* to reduce cell death.

80. (New) The method of claim 79, wherein the cell protection factor is a compound of Formula IV:



(IV)

wherein R^1 and R^2 are taken together to form an aliphatic or aromatic carbocyclic 5- to 8-membered ring, optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6 alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties, and

R^3 is selected from the group consisting of a C_1-C_6 alkyl group, a C_1-C_6 alkoxy group, and a phenyl group, wherein the alkyl group, the alkoxy group, or the phenyl group is optionally substituted with one or more straight or branched C_1-C_6 alkyl, C_1-C_6

alkoxy, hydroxy, fluoro, chloro, bromo, nitro, amino, C_1-C_6 alkylamino, and/or C_4-C_{14} aromatic or heteroaromatic moieties.

81. (New) The method of claim 80, wherein R^1 and R^2 are taken together to form a 5- or 6-membered aliphatic carbocyclic ring optionally substituted with one or more C_1-C_6 alkyl groups.

82. (New) The method of claim 79, wherein the cell death reduced is bone marrow cell death.

83. (New) The method of claim 82, wherein the cell death to be reduced is caused by exposure to at least one chemical or radiation.

84. (New) The method of claim 80, wherein the reduced cell death is bone marrow cell death.

85. (New) The method of claim 84, wherein the cell death to be reduced is caused by exposure to at least one chemical or radiation.

86. (New) The method of claim 79, wherein the mammal comprises at least one tumor.

87. (New) The method of claim 86, wherein the mammal comprises at least one $p53^+$ tumor.

88. (New) The method of claim 80, wherein the mammal comprises at least one tumor.

89. (New) The method of claim 88, wherein the mammal comprises at least one $p53^+$ tumor.

90. (New) The method of claim 79, wherein the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide.

91. (New) The method of claim 80, wherein the bone targeting agent is selected from the group consisting of a bisphosphonate, a hydroxybisphosphonate, a phosphonate, a phosphate, an aminomethylenephosphonic acid, and an acidic peptide.

92. (New) The method of claim 79, wherein the linkage is an acid-cleavable linkage.

93. (New) The method of claim 80, wherein the linkage is an acid-cleavable linkage.

94. (New) The method of claim 92, wherein the linkage is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

95. (New) The method of claim 93, wherein the linker is an enol ether, ketal, imine, oxime, hydrazone, semicarbazone, acylimide, or methylene radical.

96. (New) The method of claim 79, wherein the linkage is a hydrolytically cleavable linkage.

97. (New) The method of claim 79, wherein the linkage is an enzymatically cleavable linkage.

98. (New) The method of claim 80, wherein the linkage is a hydrolytically cleavable linkage.

99. (New) The method of claim 80, wherein the linkage is an enzymatically cleavable linkage.

100. (New) The method of claim 79, wherein the mammal is a human.

101. (New) The method of claim 80, wherein the mammal is a human.

102. (New) The method of claim 80, wherein the cell protection factor is pifithrin-β.

103. (New) The method of claim 1, wherein the cell death is reduced by at least 5%.

104. (New) The method of claim 79, wherein the cell death is reduced by at least 5%.